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In the Supreme Court of the United States

OCTOBER TERM, 1973

No. 73-168

MARKO DUROVIC, ET AL., PETITIONERS

v.

CASPAR W. WEINBERGER, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SEVENTH CIRCUIT

BRIEF FOR THE RESPONDENTS IN OPPOSITION

OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-19a) is reported at 479 F. 2d 242. The findings of fact and conclusions of law of the district court (Pet. App. 22a-25a) are reported at 327 F. Supp. 386.

JURISDICTION

The judgment of the court of appeals was entered on April 25, 1973. The petition for a writ of certiorari was filed on July 23, 1973. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

QUESTIONS PRESENTED

1. Whether Krebiozen is a "new drug" within the meaning of the Federal Food, Drug, and Cosmetic Act because it has not been generally recognized by qualified experts as safe or effective for the treatment of cancer.

2. Whether Krebiozen, which has never been the subject of an effective new drug application under the Federal Food, Drug, and Cosmetic Act, is exempt from the effectiveness requirements added to the Act in 1962.

3. Whether the record in this case presented genuine issues as to material facts which precluded disposition of the case on cross-motions for summary judgment.

STATUTORY PROVISIONS INVOLVED

1. Section 505 of the Federal Food, Drug, and Cosmetic Act, 52 Stat. 1052, as amended, 21 U.S.C. 355, provides in pertinent part:

> (a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.
>
> (b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing

of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug.

* * * * *

2. Prior to the Drug Amendments of 1962, Section 201(p) of the Federal Food, Drug, and Cosmetic Act, 52 Stat. 1041, 21 U.S.C. (1958 ed.) 321(p), provided in pertinent part:

> The term "new drug" means—
>
> (1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter it was subject to former sections 1–5 and 7–15 of this title, and if at such time its labeling contained the same representations concerning the conditions of its use; or
>
> (2) Any drug the composition of which is such that such drug, as a result of investigations to determine its safety for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

3. Section 201(p) of the Federal Food, Drug, and Cosmetic Act, as amended by the Drug Amendments of 1962, 76 Stat. 781, 21 U.S.C. 321(p), provides in pertinent part:

> The term "new drug" means—
>
> (1) Any drug * * * the composition of which is such that such drug is not generally recognized,

among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this chapter it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug * * * the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

4. Section 107(c)(4) of the Drug Amendments of 1962, 76 Stat. 789, set forth as a note following 21 U.S.C. 321, provides:

In the case of any drug which, on the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective application under section 505 of that Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

STATEMENT

Petitioners manufacture, distribute, and promote Krebiozen, a drug prescribed for use as an agent in the management of malignant tumors (Pet. App. 2a). Since the introduction of Krebiozen in 1949, petitioners and others have sought unsuccessfully to obtain administrative [1] and judicial [2] approval to market the drug.

The Federal Food, Drug, and Cosmetic Act of 1938, as amended by the Drug Amendments of 1962, requires that an administratively approved "new drug application" ("NDA") be in effect before a "new drug" may be introduced in commerce. 21 U.S.C. 355. Under the statute, the Food and Drug Administration is directed to approve an NDA only where the drug is shown to be safe and effective for its intended use.

Prior to the 1962 amendments, Section 201(p) of the Act defined "new drug" as (1) a drug not generally recognized by qualified experts as safe for its intended use, or (2) a drug recognized as safe but which had not been used to a material extent or for a material time.

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[1] New drug applications, pursuant to 21 U.S.C. 355(b), were submitted to the Food and Drug Administration for Krebiozen by Marko Durovic on April 15, 1954, and by Stevan Durovic on March 27, 31, and April 13, 1961 (see Pet. App. 4a–5a).

[2] See *Rutherford* v. *American Medical Association*, 379 F. 2d 641 (C.A. 7), certiorari denied, 389 U.S. 1043; *Tutoki* v. *Celebrezze*, 375 F. 2d 105 (C.A. 7); *Ivy* v. *Katzenbach*, 351 F. 2d 32 (C.A. 7), certiorari denied, 382 U.S. 958; *Durovic* v. *Palmer*, 342 F. 2d 634 (C.A. 7), certiorari denied, 382 U.S. 820; and *United States* v. *Bukowski*, 435 F. 2d 1094 (C.A. 7), certiorari denied, 401 U.S. 911. Each of these cases is described in the opinion below (Pet. App. 8a–9a, n. 3).

The 1962 amendments added the requirement that the drug be generally recognized by qualified experts to be effective. The amendments also included a "grandfather" clause exempting from the new efficacy requirements any drug (in the generic sense [3]) which, on the day before the amendments became effective, was "(a) commercially used or sold in the United States, (b) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (c) was not covered by an effective [NDA] * * *" (Section 107(c)(4), 76 Stat. 789, set forth as a note following 21 U.S.C. 321).

In May 1968, an investigation by the Food and Drug Administration indicated that petitioners were distributing Krebiozen in interstate commerce, in violation of Section 505(a) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 355(a). On the basis of this information, the agency issued a notice of hearing to petitioners, pursuant to Section 305 of the Act, 21 U.S.C. 335, informing them that a criminal proceeding against them was being contemplated.

On January 7, 1969, petitioners instituted the present action for a declaratory judgment that the new drug applications for Krebiozen had become effective or, in the alternative, that Krebiozen was exempted from obtaining an approved NDA by Section 107(c)(4) of the Drug Amendments of 1962. The government answered that Krebiozen is and at all times has been a new drug for which there has never been an

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[3] See *USV Pharmaceutical Corp.* v. *Weinberger*, No. 72-666, decided June 18, 1973.

effective NDA. After discovery, both parties moved for summary judgment.

In support of its motion for summary judgment, the government submitted affidavits describing the administrative history of Krebiozen and the views of qualified experts as to its safety and effectiveness as an agent for controlling malignant tumors. The affidavit of Dr. Marion J. Finkel, Deputy Director of FDA's Bureau of Drugs, stated that the agency has never approved an NDA for Krebiozen and that applications submitted for the drug in 1954 and 1961 had been refused because they were incomplete and inadequate. Petitioners never sought judicial review of those refusals. Thus, as petitioners now concede (Pet. 19), neither before nor after the 1962 amendments has Krebiozen been the subject of an effective NDA.

The affidavits of Dr. Jesse L. Steinfeld, Surgeon General of the United States, and Dr. Carl G. Baker, Director of the Public Health Service's National Cancer Institute, both qualified experts in cancer research and chemotherapy, stated that Krebiozen has never been generally recognized as safe or effective for use in the treatment of cancer.

The affidavits stated further: (1) that no medical school teaches, or has taught, that Krebiozen is a cancer treatment; (2) that no hospital associated with a medical school uses Krebiozen to treat cancer; (3) that no expert in the field of cancer believes, or has ever believed, that Krebiozen is safe or effective for the treatment of cancer; (4) that the composition of Krebiozen was not known to any expert in the field of

cancer until an FDA analysis was conducted and the results released in 1963; (5) that the chemical substances identified by the FDA analysis—a creatine derivative, an alcohol, and mineral oil—are not recognized by cancer experts as having any therapeutic value in the treatment of cancer; and (6) that cancer experts, lacking information about Krebiozen's composition and biological activity, could not have formed an opinion prior to 1963 concerning the drug's safety.

Petitioners responded by submitting the affidavits of Dr. Andrew C. Ivy, a physician who has treated patients with Krebiozen, and Marko Durovic, who asserted neither medical nor scientific qualifications (Pet. 12a–13a). Dr. Ivy and Mr. Durovic stated their personal opinions that Krebiozen is a non-toxic and beneficial drug. Neither affidavit discussed whether Krebiozen was generally recognized by qualified experts as a safe or effective cancer treatment.

The district court granted summary judgment for the government, denied petitioners' motion, and dismissed the complaint (Pet. App. 20a–21a). The court found that the evidence submitted by petitioners did not controvert the affidavits of Drs. Steinfeld, Baker, and Finkel, and that those affidavits established that Krebiozen is not now and never has been generally recognized as safe or effective for the management or treatment of malignant tumors (Pet. App. 24a). On the basis of its findings, the court concluded (1) that no approved NDA is now or has ever been effective

for Krebiozen, (2) that Krebiozen is now and has always been a new drug, and (3) that Krebiozen is not protected by the grandfather clause of the Drug Amendments of 1962 (*ibid.*).

The court of appeals unanimously affirmed (Pet. App. 1a–19a). It held that, under the law prior to 1962, a drug product used for the treatment of a life-threatening disease such as cancer was not "safe," even though non-toxic, if it was ineffective. Under that definition, Krebiozen had never been generally recognized as safe (Pet. App. 15a–17a). The court reasoned further that, even if non-toxicity were the only test for safety, Krebiozen was a new drug prior to the 1962 amendments because at that time its identity and composition were so completely unknown that it could not have been generally recognized as safe by qualified experts (Pet. App. 17a).

ARGUMENT

Petitioners contend that they need not demonstrate to the Food and Drug Administration that Krebiozen is a safe and effective cancer drug. In their view, the drug ceased to be a "new drug" because it achieved general expert recognition as a safe treatment for cancer prior to the Drug Amendments of 1962 (and, by implication, still enjoys that status). Therefore, they claim, it is exempted from the amendments' efficacy requirements by the grandfather clause in Section 107(c)(4). They further claim that the district court should not have determined these questions on a

motion for summary judgment. These contentions turn on the particular history of Krebiozen as developed on this record. They involve no issue of general importance to the administration of the Federal Food, Drug, and Cosmetic Act and do not warrant review by this Court.

1. There is no support in this record for petitioners' claim that, since its introduction in 1949, Krebiozen has somehow ceased to be a "new drug."

First, Krebiozen has never met the test for general recognition of safety under the 1938 Act. Where a drug is to be used for the treatment of a life-threatening disease such as cancer, the concept of "safety" also comprehends effectiveness. This longstanding administrative construction was explained to Congress by the Secretary of Health, Education, and Welfare in 1961: "If the drug is offered for the treatment of progressive or life-threatening diseases, such as cancer, *or* if the drug is seriously toxic or has alarming side effects, we now consider its effectiveness."[4] The medical reasons for this interpretation were set forth in this record by Drs. Steinfeld and Baker in clear and simple terms: reliance on ineffective therapy, by delaying the institution of effective therapy, permits progression of a life-threatening disease beyond the point

[4] Hearings before the Subcommittee on Antitrust and Monopoly, Senate Committee on the Judiciary, on Drug Industry Antitrust Act, 87th Cong., 1st Sess., Part 5, p. 2588 (emphasis added).

where it can be controlled and increases the likelihood of death.[5]

When it was considering whether to add an effectiveness criterion to the Act, Congress was well aware that evaluations by FDA of the safety of therapeutic agents used in treating diseases like cancer necessarily included an evaluation of effectiveness as well. Indeed, the first Senate Report on the matter, which proposed conferring on FDA the power to suspend outstanding new drug applications for lack of effectiveness, made clear that this proposal was "in no way intended to affect any existing authority of the [FDA] to consider and evaluate the effectiveness of a new drug in the context of passing upon its safety."[6]

Petitioner urges that, if this standard is correct, there would have been no reason for Congress to make "effectiveness" an express statutory requirement. But this argument ignores the fact that the old standard, under which safety would be evaluated in conjunction with effectiveness, was limited to special categories

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[5] The affidavits said (Pet. App. 16a):

"The use of an ineffective drug such as Krebiozen for the treatment of a life-threatening disease such as cancer is not a safe medical practice. Any delay in the institution of effective therapy (*e.g.*, radiation, surgery, effective chemotherapy) caused by the use of an ineffective drug allows the disease to progress beyond control. Delay means almost certain death."

[6] S. Rep. No. 1744, 87th Cong., 2d Sess., Part I, p. 15. When the FDA's proposed authority to review drugs for effectiveness was subsequently broadened, Congress gave no indication of an intent to retreat from this position. *Id.* at Part II.

such as progressive, life-threatening diseases. There was thus a broad range of drugs, allegedly therapeutic for other conditions, which were first subjected to administrative scrutiny for effectiveness by the 1962 amendments.

Second, even apart from the weight to be accorded this administrative and congressional interpretation,[7] and assuming *arguendo* that "safe" means only "nontoxic," the record does not disclose expert general recognition of Krebiozen's safety. As the court of appeals correctly concluded, "[i]t is clear that neither Dr. Ivy's affidavit nor the reports and opinions of others, reported by Durovic's affidavit, purported to assert that Krebiozen had, as of October 9, 1962, achieved general recognition among experts as safe or safe and effective" (Pet. 15a).

It may well be that individual practitioners, such as Dr. Ivy, sincerely believe that the drug is safe and beneficial in the treatment of cancer (see Pet. App. 40a–41a). But the statute prior to 1962 required *general* recognition of safety by experts qualified to evaluate the safety of drugs, and still requires it today. Unless there is a consensus among the experts that a product is safe, it simply does not meet the standards of Section 201(p). See, *e.g.*, *United States* v. *An Article of Drug . . . "Bentex Ulcerine,"* 469 F. 2d 875 (C.A. 5), certiorari denied, No. 72–1198, June 11, 1973. The record in this case is devoid of evidence showing such a consensus. On the contrary, the affidavits of Drs. Steinfeld and Baker, both spe-

[7] Cf. *Udall* v. *Tallman*, 380 U.S. 1, 16–18.

cialists well acquainted with the relevant literature and the state of expert opinion concerning cancer research, declared without contradiction that no expert in the field of cancer believes or has ever believed that Krebiozen is safe or effective for the treatment of that disease. They also stated without contradiction that prior to 1963 experts in the field lacked information about the drug's composition and biological activity and therefore could not have entertained any opinion as to its safety.

2. Since Krebiozen has never been generally recognized by qualified experts as safe for use in treating malignant tumors, it is not entitled to exemption from the "effectiveness" requirements of the 1962 amendments under the grandfather clause in Section 107(c)(4). It fails to meet the second requirement of that clause—that the product not have been a new drug at the time the amendments became effective. Accordingly, Krebiozen is subject to the same standards that apply to other "new drugs," and petitioners must demonstrate by substantial evidence that the drug is safe and effective for its intended use before it may be distributed in commerce. 21 U.S.C. 355.

3. Petitioners' contention that the case should not have been decided on cross-motions for summary judgment is without merit. Their suit was a declaratory judgment action challenging FDA's determination that their product was a new drug for which an approved NDA should have been, but was not, in effect. Petitioners were afforded a full and fair opportunity to demonstrate that a genuine issue of material

fact existed which would preclude the entry of summary judgment under Rule 56, Fed. R. Civ. P. They offered only two affidavits in response to those submitted by the government's experts. Both courts below correctly found that neither affidavit contradicted the showing by those experts that Krebiozen had never achieved general expert recognition, either as safe or as safe and effective (Pet. 15a, 23a–24a).[8]

CONCLUSION

For the foregoing reasons the petition for a writ of certiorari should be denied.

Respectfully submitted.

ROBERT H. BORK,
Solicitor General.
THOMAS E. KAUPER,
Assistant Attorney General.
HOWARD E. SHAPIRO,
LEE I. WEINTRAUB,
Attorneys.

JEFFREY B. SPRINGER,
Attorney,
Food and Drug Division,
Department of Health, Education, and Welfare.

SEPTEMBER 1973.

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[8] Petitioners' contention, presented here for the first time, that they should be granted a trial in order to test the qualifications of experts whose affidavits were submitted on behalf of the government is without foundation. The issue of expert qualifications is ordinarily a matter for the reasonable discretion of the trial court. See, *e.g.*, 2 *Wigmore on Evidence*, § 561 (3d ed. 1940). Expert opinion in the form of affidavits may be used to support a motion for summary judgment. See 6 *Moore's Federal Practice*, pp. 2801, 2812–2813 (2d ed. 1948).

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